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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,043	04/03/2000	BERND EIKMANN	21437	6651

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THE FIRM OF KARL F ROSS  
5676 RIVERDALE AVENUE  
PO BOX 900  
RIVERDALE (BRONX), NY 10471-0900

EXAMINER

STEADMAN, DAVID J

ART UNIT PAPER NUMBER

1656

DATE MAILED: 09/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/529,043

Applicant(s)

EIKMANNS ET AL.

Examiner

David J. Steadman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 07 July 2006.
- 2a) ☐ This action is **FINAL**.      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 91-108 and 110-118 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 107 and 108 is/are allowed.
- 6) ☒ Claim(s) 91-106 and 110-118 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)          |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. <u>2006.0831</u>                                     |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>5/12/06</u> .   | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### ***Status of the Application***

**[1]** A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/7/2006 has been entered.

**[2]** Claims 91-108 and 110-118 are pending in the application.

**[3]** Applicant's amendment to the claims, filed on 7/7/2006, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

**[4]** Receipt of an information disclosure statement, filed on 7/7/2006, is acknowledged.

**[5]** Applicant's arguments filed on 7/7/2006 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

**[6]** The text of those sections of Title 35, U.S. Code not included in the instant action can be found in a prior Office action.

***Claim Rejection - 35 USC § 112, Second Paragraph***

**[7]** Claims 110-118 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 110 (claims 111-115 dependent therefrom) and 116 (claims 117-118 dependent therefrom) are indefinite in that the claims attempt to claim a process of microbial production of amino acids without setting forth any steps involved in the process. According to MPEP 2173.05(q), “[a]ttempts to claim a process without setting forth any steps involved in the process generally raises an issue of indefiniteness under 35 U.S.C. 112, second paragraph.” It is suggested that applicant incorporate active, positive steps delimiting how the method is actually practiced. Also, the meaning of the term “pyruvate carboxylase is expressed with increased copy numbers” is unclear. The term “increased copy numbers” is used in the art to indicate an increase in the number of copies of a nucleic acid, however, the term would appear to refer to a polypeptide. It is suggested that applicant clarify whether the term “increased copy numbers” refers to the pyruvate carboxylase or nucleic acid encoding therefor.

***Claim Rejections - 35 USC § 102/103***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

**[8]** Claims 91-92, 95-97, 100-102, and 105-106 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Peters-Wendisch et al. (cited as reference AS in the IDS filed on 5/12/2006). The claims are drawn to an isolated nucleic acid encoding SEQ ID NO:2, including SEQ ID NO:1, a vector comprising said nucleic acid, a host cell, a method of microbial production of amino acids, and an isolated polypeptide comprising SEQ ID NO:2.

The reference of Peters-Wendisch et al. teaches Western blot analysis of a crude extract of a *C. glutamicum* strain (p. 83, Figure 30), showing assignment of a band identified as "p125," which is described at page 1 of the translation of the reference as being "the pyruvate carboxylase." As the p125 pyruvate carboxylase was separated during the Western blot, it is considered to be "isolated." This anticipates claim 106 as written.

The reference of Peters-Wendisch et al. teaches an *E. coli* transformed with a cosmid vector comprising a 40 kb *C. glutamicum* genomic insert, which comprises a 17 kb *HindIII* fragment (translation at p. 2, bottom), which hybridizes to a *C. glutamicum*

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pyruvate carboxylase gene probe (p. 85, Figure 32). This anticipates claims 91-92, 95-97, 100-102, and 105 as written.

If applicant traverses the instant rejection on the ground that the sequence of *C. glutamicum* pyruvate carboxylase and encoding nucleic acid were not known at the time of the Peters-Wendisch et al. reference, applicant's attention is directed to MPEP 2112.I, which states, "[i]n *In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that 'just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel.'"

**[9]** Claims 110-118 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Peters-Wendisch et al. (*supra*) as evidenced by Dillon et al. ("Recombinant DNA Methodology," John Wiley and Sons, Inc., New York, 1985, pp. 81-83) and Meadow et al. (*Biochem J* 72:400-407, 1959). The claims are drawn to a method of microbial production of amino acids.

The reference of Peters-Wendisch et al. discloses the teachings as described above. That a method of transformation involves culturing of an *E. coli* in a medium comprising glucose is evidenced by Dillon et al. (pp. 82-83) and that by culturing an *E. coli* in a medium comprising glucose, the *E. coli* inherently produces L-lysine is

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evidenced by Meadow et al. (paragraph bridging pp. 405-406). Thus, transforming *E. coli* with the cosmid vector comprising a *C. glutamicum* genomic insert as taught by Peters-Wendisch et al. necessarily and inherently results in amplification of the cosmid vector and thus increased copy numbers of the nucleic acid and further results in the production of L-lysine. This anticipates claims 110-118 as written.

### ***Claim Rejections - 35 USC § 103***

**[10]** Claim(s) 93-94, 98-99, and 103-104 are rejected under 35 U.S.C. 103(a) as being unpatentable over Peters-Wendisch et al. (*supra*) in view of Gubler et al. (*App Environ Microbiol* 60 :2494-2500, 1994). The claims are drawn to a bacterium of the genus *Corynebacterium*, optionally a *Corynebacterium glutamicum*, comprising the nucleic acid of claims 91, 96, and 101.

Peters-Wendisch et al. disclose the teachings as described above. Peters-Wendisch et al. further teaches that *C. glutamicum* "relies especially in the production of amino acids, which derive from precursors of the tricarboxylic acid cycle, on the activity of anaplerotic enzymes" (translation at p. 7, top) and the "pyruvate carboxylase is clearly active as anaplerotic enzyme in *C. glutamicum*" (translation at p. 9, middle). The reference goes on to state, "[i]t was shown a clear effect of the pyruvate carboxylase on the overproduction of lysine with *C. glutamicum*," particularly as "a defined pyruvate carboxylase negative mutant clearly produces less lysine than the starting strain" (translation at p. 9, bottom). Peters-Wendisch et al. does not specifically teach a

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bacterium of the genus *Corynebacterium*, optionally a *Corynebacterium glutamicum*, comprising the disclosed nucleic acid.

At the time of the invention, methods for isolating full-length *C. glutamicum* genes encoding proteins involved in L-lysine biosynthesis from gene fragments were well known in the art. For example, Gubler et al. teaches a method for cloning a full-length *C. glutamicum* pyruvate kinase gene from an internal fragment (see whole document, particularly *Materials and Methods* section at pp. 2495-2496).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Peters-Wendisch et al. and Gubler et al. to transform the pyruvate carboxylase negative mutant of Peters-Wendisch et al. with the 40 kb or 17 kb genomic fragment of *C. glutamicum* as taught by Peters-Wendisch et al. One would have been motivated to do this to confirm the presence of the *C. glutamicum* pyruvate carboxylase gene by comparing the activity of the pyc negative mutant in the presence and absence of the 40 kb or 17 kb genomic fragment of *C. glutamicum* as taught by Peters-Wendisch et al. and in order to isolate the full-length pyruvate carboxylase gene according to the method of Gubler et al. One would have a reasonable expectation of success for transforming the pyruvate carboxylase negative mutant of Peters-Wendisch et al. with the 40 kb or 17 kb genomic fragment of *C. glutamicum* as taught by Peters-Wendisch et al. because of the results of Gubler et al. Therefore, claims 93-94, 98-99, and 103-104, drawn to a bacterium of the genus *Corynebacterium*, optionally a *Corynebacterium glutamicum*, comprising the nucleic acid of claims 91, 96, and 101 would have been obvious to one of ordinary skill in the art at the time of the invention.



### ***Deposit Requirement***

**[11]** Claim 107 (claim 108 dependent therefrom) is drawn to a novel vector contained in the microorganism deposited as DSM 12893. According to the deposit receipt filed 3/1/2005, the microorganism has been deposited under the terms of the Budapest Treaty. Further, applicant's representative has provided a statement that the deposited microorganism will be irrevocably and without restriction or condition released to the public upon the issuance of a patent (3/1/2005 response at p. 6).

### ***Conclusion***

**[12]** Status of the claims:

Claims 91-108 and 110-118 are pending.

Claims 91-106 and 110-118 are rejected.

Claims 107-108 appear to be in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Thurs and alternate Fri, 7:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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A handwritten signature in black ink, appearing to read 'D.J. Steadman', with a long horizontal flourish extending to the right.

David J. Steadman, Ph.D.  
Primary Examiner  
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